Is Dressler Syndrome Dead?*

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Post-acute myocardial infarction (AMI) syndrome was first described by Dressler in 1956. Its incidence has decreased in the reperfusion era, most likely because of the extensive use of thrombolysis and coronary balloon angioplasty, therapies that dramatically decreased the size of myocardial necrosis. The authors suggest that drugs that have been prescribed in previous decades as the post-AMI “standard-of-care,” such as angiotensin-converting enzyme inhibitors, β-blockers, and statins, may also play an important role in the disappearance of Dressler syndrome due to their immunomodulatory effects. (CHEST 2004; 126:1680–1682)

Key words: inflammatory reaction; myocardial necrosis; pericardial effusion
Abbreviations: ACE = angiotensin-converting enzyme; AMI = acute myocardial infarction; DS = Dressler syndrome

Dressler’s description,1 > 40 years ago, of a clinical entity following an acute myocardial infarction (AMI) continues to be indelibly evoked at bedside and in the standard cardiology literature. Clinical features of this post-AMI syndrome include fever, chest pain, pericarditis, pleurisy occurring 2 to 3 weeks after the AMI, and a tendency for recurrence.2 Prior to the reperfusion era, the reported incidence of Dressler syndrome (DS) ranged from 1 to 5% of patients with AMI.2–5 The incidence of DS, however, has decreased in the reperfusion era, most likely due to the widespread use of therapy with thrombolysis6,7 and balloon angioplasty.8 Supporting this, in a prospective study of 201 patients with AMI who had undergone thrombolysis, Shahar et al9 found that no patient showing clinical signs of early reperfusion had DS. The only patient who developed DS in the latter study had had an extensive anterior AMI without evidence of reperfusion. Before the reperfusion era, Lichstein and colleagues10 suggested that the decreased incidence of DS was related to the modification of the treatment of patients with AMI. The use of novel therapies, such as nonsteroidal antiinflammatory agents, steroids, and salicylates, and the decreased use of oral anticoagulants were evoked. In addition to the two mechanisms discussed above, which may account for the observed decrease in the incidence of DS,9,10 the authors propose a third hypothesis. We think that drugs that have been prescribed in previous decades as post-AMI “standard-of-care” may also play an important role in the disappearance of DS.

Etiology of DS
Before the Era of Coronary Reperfusion

Several pathogenic mechanisms have been proposed for DS, including local inflammation,11 autoimmune reaction,12 and latent viruses.13 Irritant pericarditis due to the presence of blood in the pericardial space induced by anticoagulation therapy was at that time anticipated as a likely mechanism.1 However, anticoagulation therapy could not be related to all cases since > 25% of patients in the original report of Dressler1 did not receive anticoagulants.2 In addition, nowadays, a significant number of patients still receive anticoagulants after experiencing anterior AMIs,14 yet DS is not observed.
in this patient population. These two facts seem to rule out anticoagulants as the drugs playing a major role in the pathogenesis of DS.

Since the Era of Coronary Reperfusion

The decrease of the incidence of DS has been viewed as another beneficial effect of early and aggressive coronary reperfusion therapy, which decreased mortality and improved cardiac function.9 It was postulated9 that the diminution of the infarct size and the shortened time of exposure of the myocardial antigens to the immune system accounted for the decreased incidence of DS. Although the reduction in both the number of patients with AMI and in the infarct size following coronary reperfusion may play a role in the observed decrease of the incidence of DS,15,16 this can hardly explain the quasi-complete disappearance of the syndrome. Indeed, even in the reperfusion era, a significant number of patients will develop large AMIs due to unsuccessful or late reperfusion. The quasi-absence of DS in this patient population calls for another mechanism to explain their protection against DS.

The Authors’ Hypothesis

DS is a recurrent immunoinflammatory syndrome that has similarities with other syndromes occurring after myocardial injury, such as postcardiotomy syndrome and posttraumatic pericarditis.17 Following myocardial injury or AMI, myocardial antigens are exposed and/or released, and, in some cases, an immune complex can form. This immune activation triggers a local inflammatory reaction, and may involve remote organs such as the pleura and synovia, due to molecular mimicry and immune cross-reactions.12 The time needed for the immune reaction to develop may account for the observed latency period of 2 to 3 weeks between the AMI and the onset of DS. The duration of DS may be explained by the limited time during which myocardial antigens are exposed to the immune system and corresponds grossly to the time necessary for the myocardium to heal after an AMI. Interestingly, the hypothesis proposed herein suggests that this immune reaction has been minimized by novel therapies administered in the last 1 or 2 decades in the vast majority of patients who have experienced AMIs. These therapies include the use of angiotensin-converting enzyme (ACE) inhibitors, statins, and β-blockers. All of these drugs have been proposed to carry immunomodulatory properties.18–22 These drugs also lower the risk of recurrent AMI in addition to their effect on all-cause mortality. A direct relationship between systemic inflammation and myocardial ischemia has been highlighted by several authors.23–27 Interestingly, Gullestad et al19 have shown that circulating levels of proinflammatory cytokines were reduced by high doses of ACE inhibitors in patients with heart failure. Other authors demonstrated that ACE inhibitors reduced myocardial injury in cell cultures and in isolated hearts.18 In similar studies, β-blockers have been shown to decrease circulating levels of proinflammatory cytokines.20,22 Statins, a new class of lipid-lowering drugs that reduces cardiovascular-related morbidity and mortality,28,29 are now widely used for treatment after an AMI. Although these agents have not directly been shown to decrease the levels of systemic proinflammatory mediators in patients with AMI, they carry unequivocal protective antiinflammatory and immunomodulatory properties.21 Moreover, statin therapy has been found to lower levels of C-reactive protein25,30 and Nahrendorf et al31 have demonstrated that left ventricular remodeling after AMI was profoundly changed by statin treatment in rats.

Another explanation for the post-AMI syndrome could be the close proximity between the myocardium and the pericardium. The inflammatory process that affects the cardiac muscle could propagate a nonspecific inflammatory response to the neighboring pericardium. However, the usual latency period of 2 to 3 weeks between the AMI and the onset of DS makes this hypothesis less likely, and corresponds more to the pathogenesis of the acute pericarditis observed within the 5-day period after the AMI.

Summary

Historically, attempts to understand the quasi-complete disappearance of the DS have focused on early coronary reperfusion therapy, and less attention has been given to drugs with immunomodulatory properties. We hypothesize that the most likely disappearance of DS following a correctly treated AMI is related to drugs that have a strong defensive effect by virtue of diverse antiinflammatory effects.

References

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CHEST / 126/5 / NOVEMBER, 2004 1681